



## CAROTID MASTERCLASS

# Neuro-rescue during Carotid Stenting

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**Abstract** This paper deals with the treatment of acute neurological complications that may occur during carotid angioplasty with stenting. Endovascular ‘neurorescue’ techniques include mechanical thrombus removal (using retrieval devices, aspiration catheters, and wire or balloon fragmentation) and local and intra-arterial thrombolysis. The treatment of acute thrombosis and dissection during carotid artery and stenting will also be discussed.

Knowledge of these additional skills is essential to increasing the safety of carotid stenting procedures.

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## Introduction

Due to increasing Interventionist experience in conjunction with optimization of pharmacotherapy before, during and after carotid angioplasty with stenting (CAS) and the development of dedicated tools (stents, embolic protection devices), CAS has become a much safer procedure compared with the early 1990s. However, there still remains situations when immediate treatment of acute neurological complications becomes necessary. These complications generally follow a reduction of cerebral blood flow due to embolization, thrombosis, or dissection in the ipsilateral internal carotid artery (ICA) or its branches. The fundamental aim of treating these complications is to recanalise the occluding lesion with reperfusion of the

distal arterial bed as soon as possible in order to salvage as much penumbral tissue as possible, whilst avoiding haemorrhagic transformation.<sup>1,2</sup>

## Procedural embolization

Embolization can occur as micro-emboli or macro-emboli. A major reduction in micro-embolization can be achieved by optimization of pre-operative pharmacological treatment using anti-coagulant and antiplatelet therapy (e.g. Gp-IIb/IIIa inhibitors). This allows for plaque stabilization prior to performing the procedure. Using filter-type protection devices, the overall number of micro-emboli (i.e. emboli smaller than the pore-size of the filter) increases. However, embolic protection devices do seem to reduce the number of macro-embolic events (i.e. emboli larger than the pore-size).<sup>3,4</sup> Micro-emboli generally do not cause any acute neurological deficit, but the long-term effects (e.g. on cognition) remain unknown.

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Despite the use of protection devices, however, macro-emboli still occur and are related to incomplete deployment and/or vessel wall appositioning of the filter devices,<sup>5,6</sup> or they occur in cases of insufficient aspiration of debris in the so-called dead-space when using distal balloon protection devices. Finally, macro-embolization can occur in a small number of patients because embolic protection devices could not be used for technical reasons or patient intolerance (e.g. balloon protection devices).<sup>7</sup>

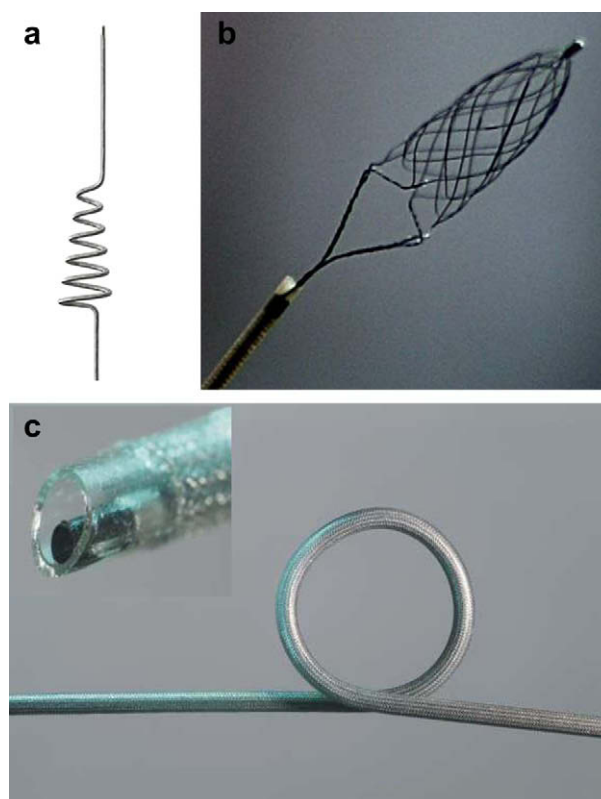
Large emboli can be removed mechanically, or an attempt can be made to dissolve them using thrombolytic therapy. Mechanical removal of an embolus is particularly helpful in cases where the embolus is likely to be derived from the atherosclerotic plaque (cholesterol, lipid debris<sup>8,9</sup>), i.e. unlikely to be effectively dissolved by thrombolytic agents.

### Mechanical removal of an embolus

Mechanical removal has a theoretical advantage over thrombolytic therapy because it carries a lower risk of bleeding (especially in cases where hyperperfusion is likely to occur) and because the material that is dislodged is expected to be more organized and/or non-thrombotic. In the past, mechanical thrombectomy devices failed in the intracranial vessels, primarily because of damage to the vessel walls. Nowadays, safe mechanical removal of embolic material from the main branches of the internal carotid artery (i.e. until the proximal part of the M2-segment) is possible using specific neuro-interventional retrieval systems.

A number of devices are now available (Fig. 1) and can be divided into two major subgroups according to their mode of action. Proximal devices (e.g. aspiration catheters) apply a vacuum force to the proximal aspect of the embolus. Distal devices (spiral-shaped or basket-like devices) are advanced through the thrombus, thereby allowing force to be applied to the distal segment of the thrombus. The latter devices are typically introduced through the pre-existing guiding catheter or long introduction sheath and are advanced beyond the point of occlusion in an un-deployed state using a microcatheter.

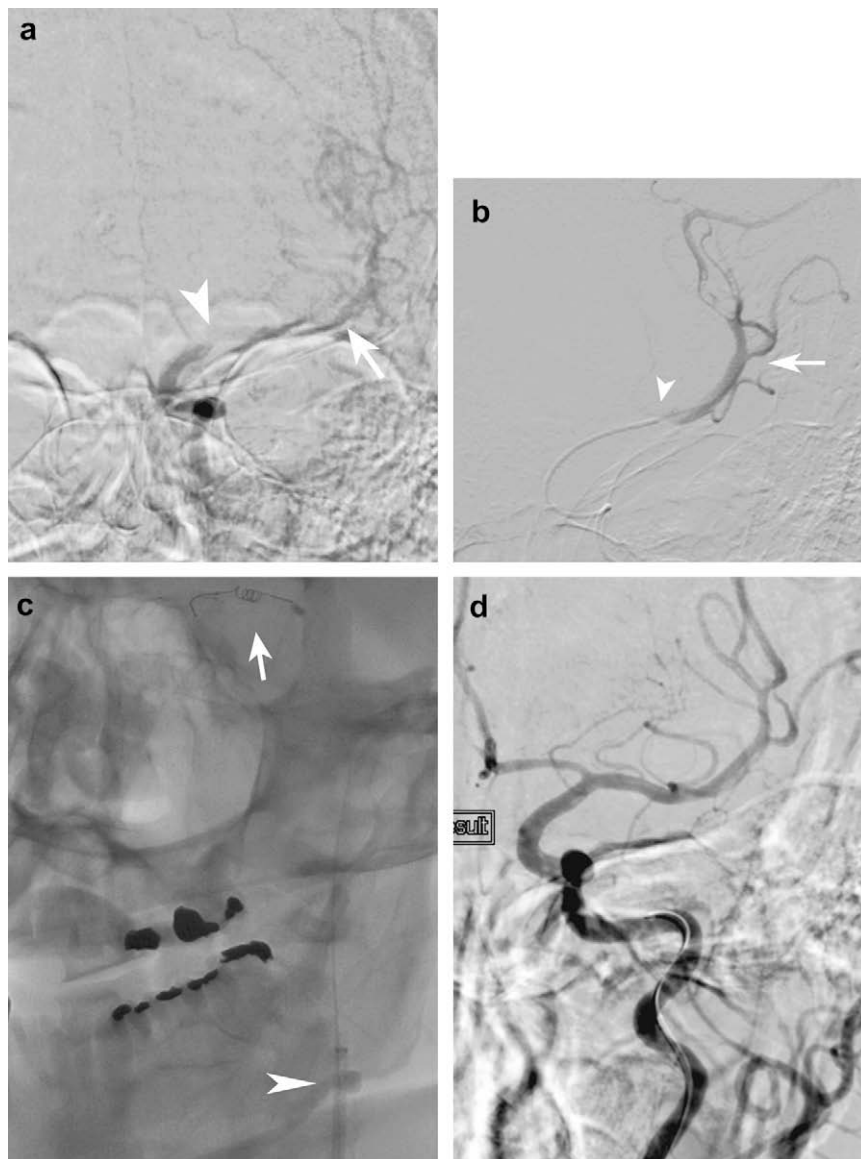
The two mechanical retrieval systems currently available (and approved) on the European market are the Merci Retriever System (Concentric Medical, Mountain View, CA) and the Catch device (Balt Extrusion, Montmorency, France). The *Merci Retriever System* consists of the Merci Clot retrieval device, the Merci balloon guide catheter, and the Merci microcatheter. The retrieval device is a tapered wire of thermal memory-encoded nitinol with 5 helical loops of decreasing diameter (Fig. 1a). The balloon guide catheter needs to be placed in the common or internal carotid artery. Through this catheter, the microcatheter is then advanced beyond the point of embolic occlusion (Figs. 2 and 3). Subsequently the Merci retriever is advanced through the microcatheter until 2–3 helical loops are deployed. The retriever is then withdrawn until contact with the embolus is established. The microcatheter is then withdrawn enabling the remaining loops of the retrieval device to be deployed. Next, the balloon of the guiding catheter is inflated to block or reduce antegrade flow in the treated vessel and five clockwise rotations are applied to the Merci retriever in order to fully ensnare the embolus.



**Figure 1** Overview of some of the devices currently available for mechanical retrieval of macro-emboli from the intracranial circulation. (a), Merci retriever device (Concentric Medical, Mountain View, CA). (b), Catch thrombus retriever system (Balt Extrusion, Montmorency, France). (c), Proboscis Rx catheter (Medical Braiding AG, Giswil, Switzerland). Note the large inner lumen with a separate channel for rapid exchange wire and kink resistance due to micro-braiding.

Finally, continuous aspiration is applied to the balloon guide catheter while the retriever and microcatheter are withdrawn simultaneously. Figs. 2 and 3 illustrate the successful use of the Merci Retriever System in the carotid and vertebrobasilar territories. This manoeuvre can be repeated up to six times<sup>10</sup> and adjunctive procedures (e.g. intra-arterial thrombolysis) can be performed where necessary. The clinical efficacy of the Merci retriever has been reported in the MERCI trial and in a large single-centre cohort in patients suffering from acute ischemic stroke (not related to carotid angioplasty).<sup>10–14</sup>

The *Catch thromboembolectomy device* (Figs. 1b and 4) comprises a self-expandable basket with radiopaque markers (identifying the distal tip and the proximal opening of the device) and a braided microcatheter (Vasco +). The system should be used in conjunction with a guiding catheter of at least 6F. The microcatheter is advanced together with the guidewire to a point that is located at least 2 cm distal to the occlusion. After removal of the guidewire, the Catch system is advanced through the occlusion, taking care that the tip of the basket does not protrude beyond the tip of the microcatheter. The basket is then opened by withdrawal of the microcatheter. Upon full opening of the basket, the whole system is withdrawn into the guiding



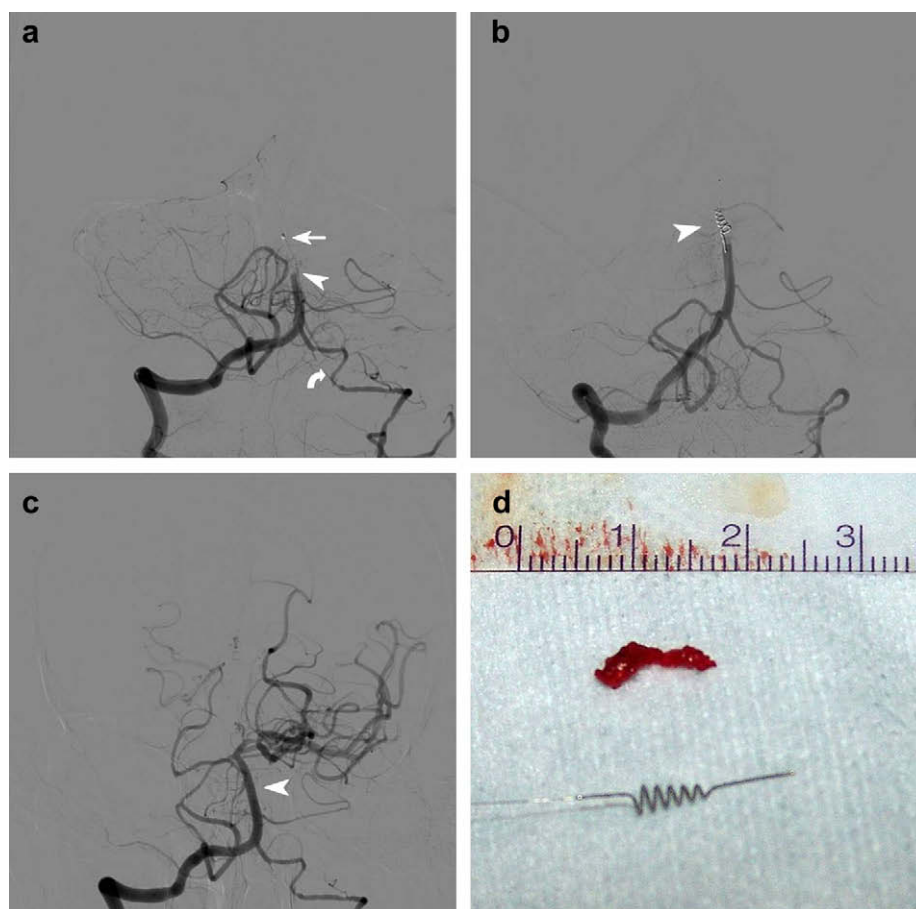
**Figure 2** How to deal with acute embolic occlusion of the middle cerebral artery (MCA) using the Merci retriever device. (a), Selective angiography of the left internal carotid artery in a patient with acute occlusion of the left MCA (arrowhead) that was not related to a carotid stenting procedure. Note the poor distal perfusion (arrow). (b), Supra-selective angiography demonstrating tip of microcatheter (arrowhead) beyond the point of occlusion. Distal MCA flow is better demonstrated (arrow). (c), Fluoroscopic image demonstrating deployment of Merci retriever device in the left MCA (arrow). Note the balloon guiding catheter, with balloon inflated (arrowhead). (d), Completion angiography demonstrating complete restoration of flow after mechanical thrombectomy. (Images provided courtesy of Jan Albert Vos, MD, Nieuwegein, The Netherlands.)

catheter (Fig. 4). A special re-sheathing hub is included in the package to allow for multiple attempts to retrieve embolic material.

*In vivo* testing using an animal model has shown that distal mechanical devices are associated with a relatively higher risk of spasm, but require significantly fewer passages to achieve complete recanalization of the occluded segment. They do, however, take longer than proximal aspiration devices.<sup>15</sup> A comparison of the two commercially available distal devices revealed a higher fragmentation rate of thrombus using the Catch device,<sup>16</sup> with both devices having the disadvantage of compressing the thrombus when pulled back. Although not specifically

advised by the manufacturer, use of the Catch device in conjunction with proximal balloon occlusion and aspiration during device retrieval seems to be essential in order to reduce the number of distal emboli, and is therefore recommended by some authors.<sup>16</sup>

Potential sources of failure of mechanical retrieval devices are excessive tortuosity of the arteries to be negotiated, and the presence of a severe stenosis along the pathway to the embolic occlusion.<sup>11</sup> Complications of retrieval devices include dissection (mainly related to the use of the occlusion balloon with the Merci device), embolization into a previously uninvolved vessel segment and (intracranial) vessel perforation. Fracture of the coil of



**Figure 3** How to deal with acute occlusion of the basilar artery using the Merci retriever device. (a) Selective angiogram of the vertebrobasilar system demonstrating occlusion of the basilar artery (arrowhead). The tip of the microcatheter lies within the occlusion (arrow). Note the hypoplastic left vertebral artery (curved arrow). (b), Selective angiography performed with the Merci retriever in place (arrowhead). (c), Completion angiography showing recanalization of the basilar artery (arrowhead), and its distal branches. (d), Image of removed clot and Merci retriever after removal from guiding catheter. (Images provided courtesy of Jan Albert Vos, MD, Nieuwegein, The Netherlands.)

the Merci retriever (first generation device) and detachment of the tip has also been described.<sup>10</sup>

#### Aspiration of an embolus/thrombus

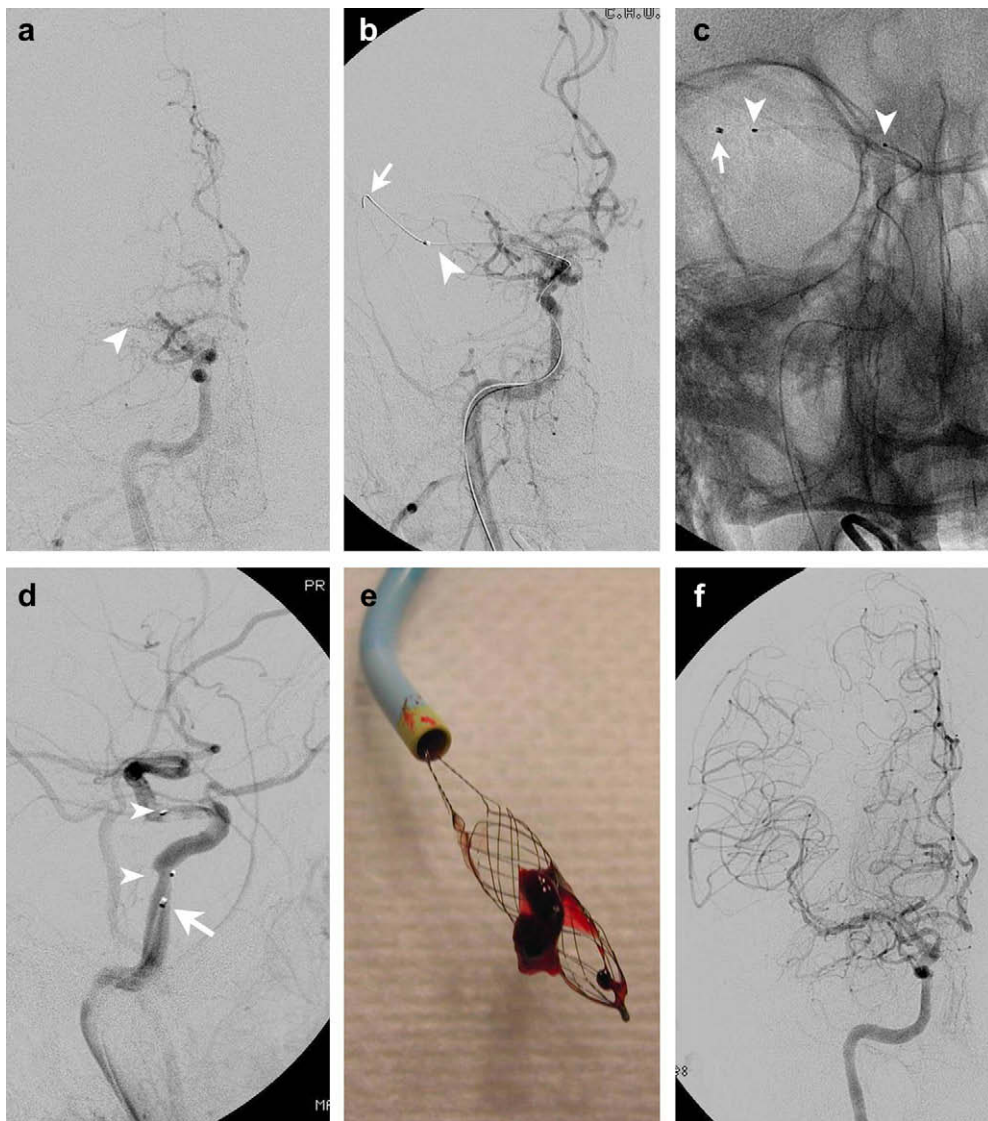
Aspiration of thrombus from the common carotid artery or cervical portion of the internal carotid artery using diagnostic or guiding catheters (diameter of 4F–7F) has been well described.<sup>17–19</sup> When using diagnostic catheters, it is important to use catheters without sideholes, otherwise no vacuum can be obtained. The catheter should be advanced until it smoothly contacts the thrombus, and negative pressure is then applied using a 50 mL syringe. For aspiration thrombectomy at the intracranial level, several microcatheters are available (Vasco + 35 (Balt); Proboscis (Medical Braiding AG, Giswil, Switzerland); QuickCat (Kensey Nash Corporation, Exton, PA); Diver (Invatec, Roncadelle, Italy); and Export (Medtronic, Minneapolis, MN)). Catheters used for this purpose (Fig. 1c) should have a large inner lumen and should be kink-resistant (provided by micro-braiding). If microcatheters are to be used for aspiration, smaller syringes (<10 mL) should be used. *In vivo* experiments have demonstrated similar effectiveness regarding thrombus removal (as compared with distal

devices), although the use of aspiration catheters is associated with an increased number of attempts to secure recanalization.<sup>15</sup> One important advantage of aspiration catheters is that they can be used in situations where there is limited space distal to the occlusion. In this situation, the use of distal retrieval devices is precluded. An example of aspiration thrombectomy in the vertebrobasilar system is illustrated in Fig. 5.

#### Fragmentation techniques

In the acute situation (especially in the absence of dedicated retrieval devices), restoration of antegrade flow can be achieved by simply fragmenting the occluding embolus using a balloon angioplasty catheter or by guidewire manipulation.<sup>20</sup> Wire fragmentation should be performed using a flexible tip hydrophilic guidewire (0.008"–0.010"). The wire tip should be formed into a J-shape in order to avoid vessel wall perforation. Penetration and fragmentation of the thrombus can be achieved by gently advancing and rotating the wire.<sup>21</sup> Balloon angioplasty, however, tends to be relatively ineffective, due to the spongy nature of the clot/embolus that leads to instant recoil.<sup>1</sup> In the event of recoil, additional stent placement at the level of





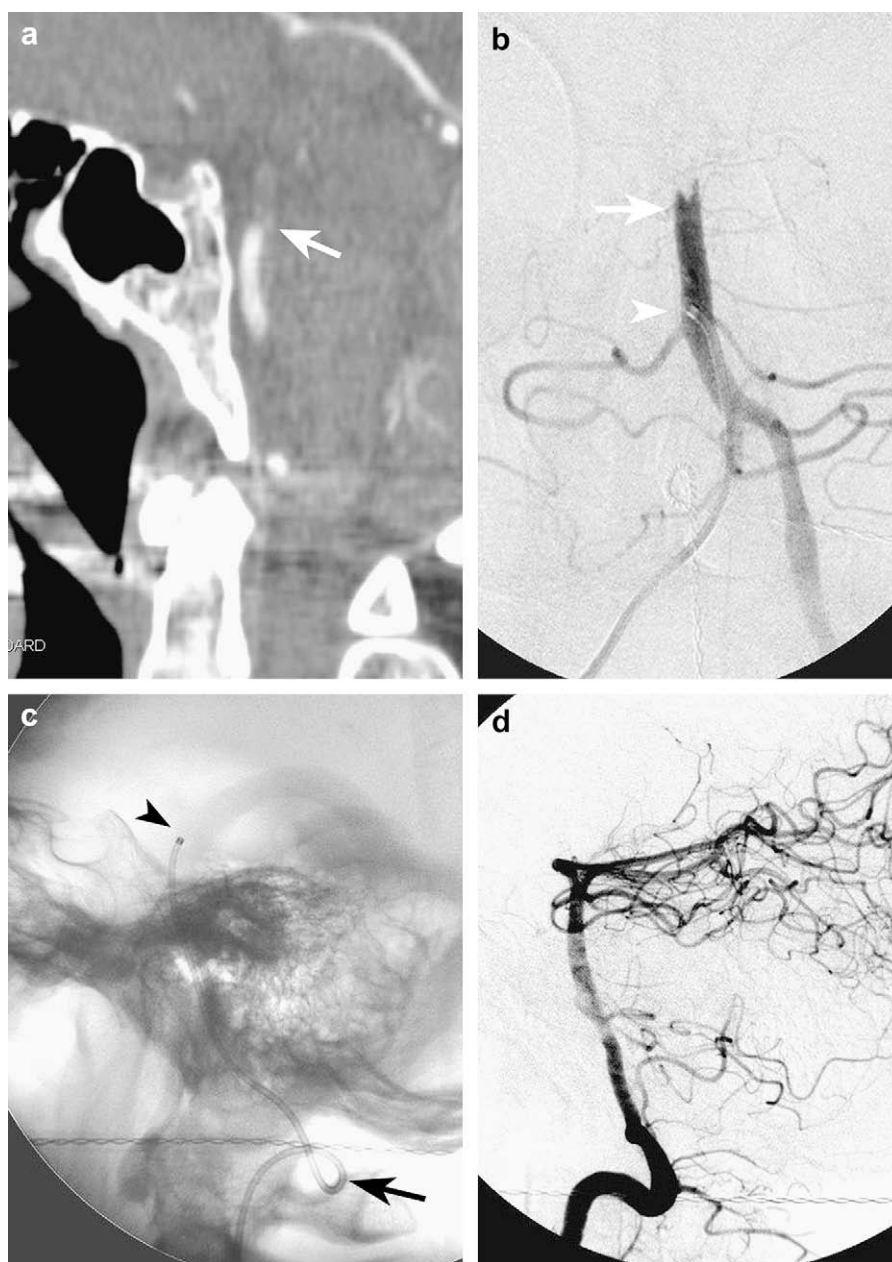
**Figure 4** How to deal with acute occlusion of the middle cerebral artery using the Catch device (a), Selective angiography of the right internal carotid artery in a patient presenting with acute stroke (not related to a carotid stenting procedure) demonstrating occlusion of the right middle cerebral artery (arrowhead). (b), Selective angiography of the right internal carotid artery after passage of microguidewire (arrow) and microcatheter (arrowhead) beyond the point of occlusion. (c), Fluoroscopic image demonstrating position of microcatheter (arrow) and retrieval device (Catch) with its markers (arrowheads), the retrieval device is still in its non-deployed state. (d), Selective angiography after deployment of the retrieval device (markers indicated with arrowheads) and after withdrawal of the device and microcatheter (arrow) into the siphon of the right internal carotid artery. (e), Image of Catch retriever device and guiding catheter after complete withdrawal, demonstrating the presence of fresh clot in the basket. (f), Selective control angiography of the right internal carotid artery demonstrating complete restoration of flow. (Images courtesy of Professor René Chapot, Limoges, France.)

the (residual) embolus can be performed.<sup>22</sup> In order to be able to reach the lesion, flexible stents and stent delivery systems should be used. Best suited for this purpose are Co–Cr alloy stents used in percutaneous coronary interventions.<sup>23</sup> The main disadvantage of the fragmentation technique (and to a lesser extent stenting) is the relatively high risk of distal embolization.

#### Intra-arterial thrombolysis

Intra-arterial thrombolysis has been shown to be an effective therapy for acute thrombotic occlusion of cerebral

vessels and, as distinct from the retrieval devices, can be used for small calibre distal occlusions in M2, M3 and higher order MCA branches.<sup>24</sup> The site of occlusion, type of thrombus and presence of leptomeningeal collateralization influences the likelihood of recanalization success. Typically, occlusions of the proximal carotid terminus and the M1 segment of MCA respond poorly to intra-arterial thrombolysis, mainly due to the large clot burden requiring a much longer time for full enzymatic digestion.<sup>1</sup> Although a thrombus/embolus in the MCA may be successfully treated with lysis, clinical success may be negatively



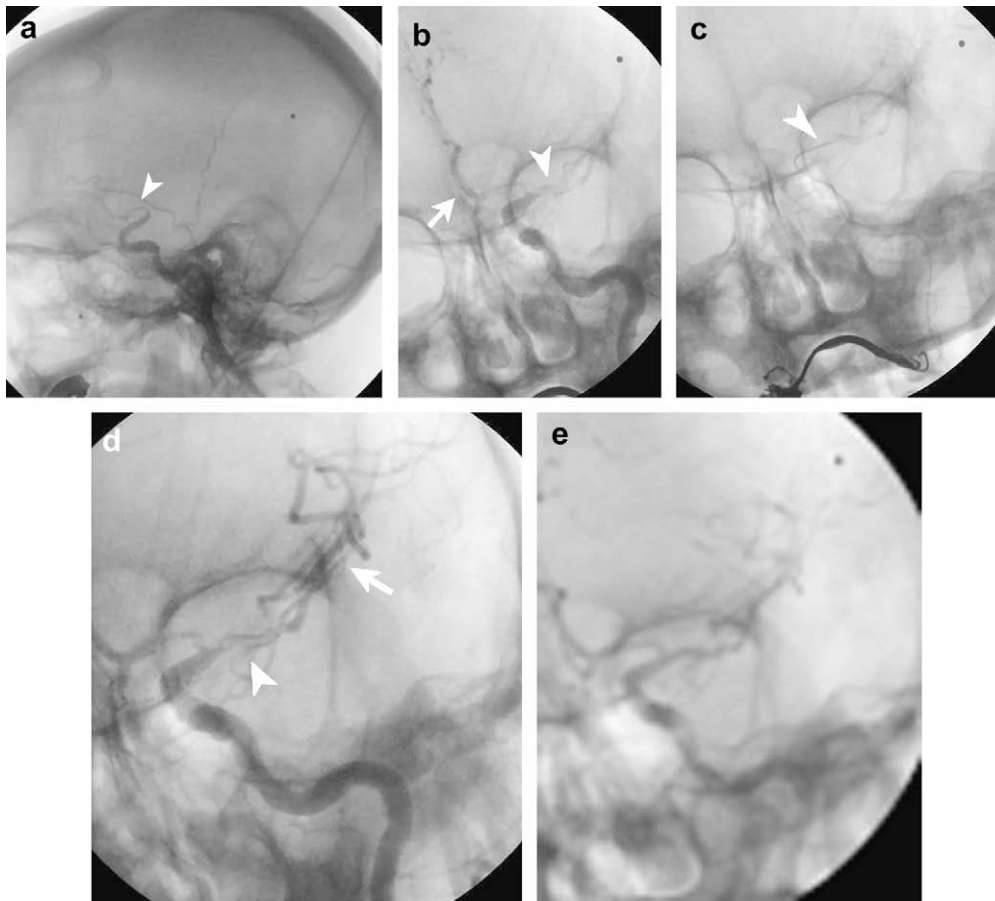
**Figure 5** Aspiration thrombectomy. (a), Patient with acute vertebrobasilar stroke; coronal MPR reconstruction of CT angiography demonstrating occlusion of the basilar artery (arrow). (b), Digital subtraction angiography in the same patient confirming embolic occlusion of the basilar artery (arrow); a microcatheter has been advanced into the basilar artery (arrowhead). (c), Fluoroscopic image in lateral projection after advancement of the catheter with tip of the catheter now against the embolus (arrowhead); note the tortuosity in the distal part of the vertebral artery (arrow). (d), Completion angiography demonstrating complete restoration of flow. (Images How to deal with acute embolic occlusion of the middle cerebral artery using the Merci retriever device courtesy of Professor Gerhard Schroth, Bern, Switzerland.)

influenced by non-recanalization of smaller lenticulostriate branches. Commonly used thrombolytic agents include urokinase and recombinant Tissue Plasminogen Activator (rTPA) and are delivered through a super-selectively placed microcatheter.

An infusion microcatheter (<3.0F) with a single end hole should be placed into the proximal one third of the thrombus using a steerable microguidewire (Fig. 6). Using a so-called coaxial catheter technique, the microcatheter

is advanced through an Y-connector attached to a diagnostic catheter with a lumen of at least 0.038". The Y-connector also permits continuous flushing of the microcatheter with heparinized saline. If it proves impossible to position the microcatheter within the thrombus, the tip of the microcatheter needs to be placed as close to the proximal aspect of the occlusion as possible.

A super-selective angiogram is then performed via the microcatheter in order to confirm proper positioning of the



**Figure 6** Intra-arterial thrombolysis. (a), Selective angiography of the left internal carotid artery (lateral projection) in a patient suffering from an acute hemispheric neurological deficit after coronary angiography. The arrowhead marks the embolus occluding the left middle cerebral artery. (b), Selective angiography of the left internal carotid artery (antero-posterior projection) in the same patient; note presence of flow in the anterior cerebral artery (arrow) and absence of flow in the middle cerebral artery (arrowhead). (c), Fluoroscopic image after positioning of microcatheter (arrowhead) for local, intra-arterial thrombolysis. (d), Angiographic image after administration of 500,000 U of urokinase; partial recanalization (arrowhead) of the M1 segment of the middle cerebral artery is seen with flow into peripheral (M2) branches (arrow). (e), Completion angiography demonstrating complete restoration of flow. The clinical course was uneventful with complete regression of neurological symptoms.

catheter (Fig. 6). High-dose urokinase regimens are generally administered (500,000 IU urokinase with half being administered as a single initial bolus). Alternatively, a continuous infusion (without bolus) of up to 250,000 units of urokinase over 90 min can be performed.<sup>21</sup> rTPA may be given as a 5-mg bolus followed by slow-infusion (maximum dose 20 mg).<sup>25</sup> It is of utmost importance to perform regular angiograms during the period of thrombolysis (e.g. every 15 min) and to continue thrombolytic therapy until complete recanalization has been achieved (up to a maximum of 1 h). If any of the proximal thrombus dissolves, the tip of the microcatheter has to be advanced into the proximal portion of any remaining clot. Mechanical disruption of the clot can also be performed in those situations where no lytic activity is observed.

As mentioned previously, intra-arterial thrombolysis increases the risk of hemorrhagic complications. In the PRO-ACT II trial of thrombolytic therapy, intracranial hemorrhage within 24 h occurred in 35% (38/108) of treated patients as compared with 13% (7/54) of control patients ( $P = 0.003$ ).<sup>24</sup> Selective intra-arterial administration of

5 mg abciximab (ReoPro, Lilly Pharmaceuticals, Indianapolis, IN, USA) followed by a bolus of 5 mg abciximab intravenously has also been demonstrated to be effective in the treatment of acute neurological sequelae due to distal embolization after carotid artery angioplasty and stent placement.<sup>26</sup> High recanalization rates (>75%) can be achieved, when combining endovascular techniques such as mechanical fragmentation of the thrombus, thromboaspiration, percutaneous transluminal angioplasty, and implantation of stents.<sup>27</sup>

#### Thrombosis during CAS

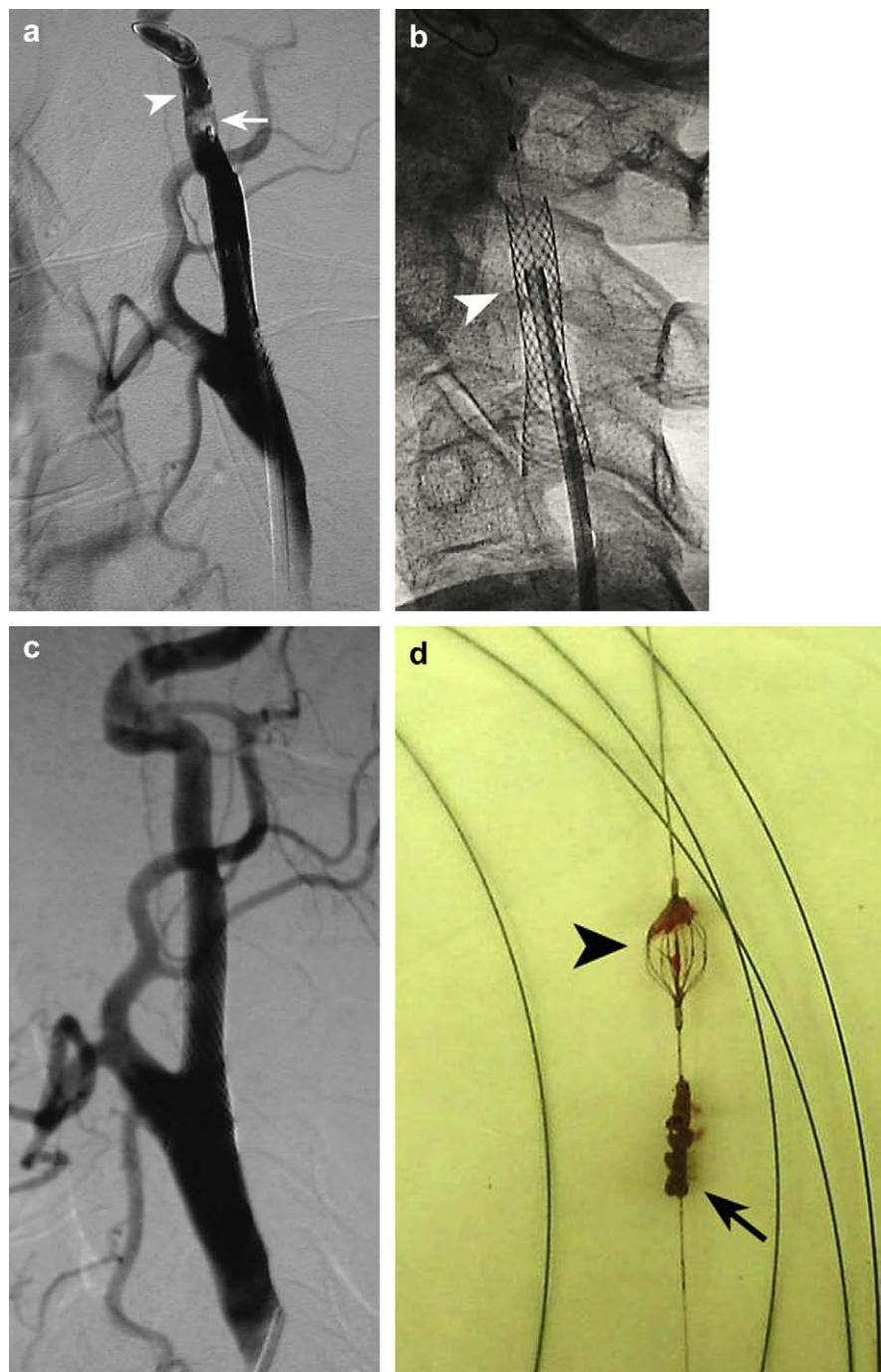
Thrombosis occurring during the CAS procedure seems to be associated with the use of embolic protection devices (e.g. filter devices), but acute thrombosis of the stented target lesion has also been described. In addition, a large embolic load may completely block the filter device leading to proximal stasis of blood. There have also been cases where thrombus forms on the wires of the filter system<sup>28</sup> despite maximum anti-coagulant therapy. Treatment consists of local administration of abciximab or aspiration of thrombus



followed by retrieval of the filter device using the guiding catheter or sheath already in place<sup>29</sup> (Fig. 7). Care should be taken not to try to close the filter system completely, as its embolic–thrombotic contents may be squeezed out and embolize distally.

Acute stent thrombosis is a rare (0.5–2%<sup>30</sup>) but potentially fatal complication. It seems to be related to the lack

of (pre)treatment with combination antiplatelet therapy,<sup>31</sup> although cases occurring despite pre-treatment with dual antiplatelet therapy have been described.<sup>32</sup> Treatment consists of intra-arterial thrombolysis or administration of intra-arterial abciximab.<sup>30,31,33</sup> Intra-arterial thrombolysis may involve administration of either urokinase or rTPA using the dosage regimens described above.<sup>34</sup> A successful



**Figure 7** Treatment of thrombus forming within an embolic protection device after CAS. (a), Periprocedural angiography demonstrating filling defect (arrow) proximally from embolic protection device (arrowhead); filling defect represents thrombus. (b), Non-subtracted image of stent and filter device; the guiding catheter has already been advanced to the level of the stent. (c), Angiogram after thromboaspiration and retrieval of the embolic protection device using the guiding catheter confirming patency of the internal carotid artery. (d), Close-up of embolic protection device (arrowhead) showing presence of thrombotic material (arrow) on the guidewire despite full antiplatelet and anticoagulation therapy.



dosage-scheme of 0.25 mg/kg of abciximab intra-arterially, followed by a continuous intravenous infusion (9 µg/min for 12 h) has been reported.<sup>33</sup> Alternatively intra-carotid injection of 5 mg rTPA, followed by systemic administration of 5 mg rTPA and intra-carotid administration of a half-dose bolus of abciximab (0.125 mg/kg) can be performed (so-called facilitated thrombolysis).<sup>32</sup>

In rare situations where endovascular therapy and/or systemic pharmacological treatment does not resolve the occlusion rapidly, conversion to surgery using either thrombendarterectomy with stent removal and patch closure or thrombectomy using aspiration after transverse arteriotomy of the ipsilateral common carotid artery should be considered.<sup>35</sup>

### Dissection during CAS

Dissection during CAS is rare and usually related to stent placement, balloon angioplasty and distal balloon embolic protection devices.<sup>7</sup> In cases where flow reduction is limited, a wait-and-see policy should be employed. In situations where there is severe flow impairment, treatment consists of either insertion of a second stent<sup>7</sup> or urgent surgical repair.<sup>36</sup>

### In Conclusion

The majority of CAS procedures usually proceed without any major complications. However, it is important to be familiar with at least one mechanical neuro-interventional retrieval system and one type of microcatheter when performing carotid artery stenting. Knowledge of these devices must be acquired in advance and not left to the emergency situation. Similarly, the CAS operator should have Urokinase, rTPA and/or abciximab available and be aware of the dosage and administration regimes. Adding these additional skills to the armamentarium of the interventionalist will increase the safety of carotid stenting procedures even further.

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